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    Andrew P. Feinberg
Application No.: 10/629,318
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AMENDMENTS TO THE CLAIMS

Please amend claims 1, 7, 8, 10, 17, and 20, as set forth below. Please cancel claim 19, and withdraw claims 9, 12, and 21, without prejudice or disclaimer.

The current listing of claims replaces all prior listings.

1. (Currently Amended) A method for identifying loss of imprinting <u>(LOI)</u> of the IGF2 gene in a subject with <u>colorectal cancer</u>, comprising analyzing a biological sample from the subject for hypomethylation of a differentially methylated region (DMR) of at least one of the H19 gene and the IGF2 gene[[,]] <u>and</u>

    <u>detecting hypomethylation of the DMR in the subject, wherein detection of hypomethylation of the DMR in the subject correlates with loss of imprinting (LOI)</u>.

2. (Original) The method of claim 1, wherein the method comprises analyzing the biological sample for hypomethylation of a DMR of the IGF2 gene comprising SEQ ID NO:1 or a polymorphism thereof, or a fragment of SEQ ID NO:1 or a polymorphism thereof.

3. (Original) The method of claim 1, wherein the method comprises analyzing the biological sample for hypomethylation of a DMR of the H19 gene comprising SEQ ID NO:6 or a polymorphism thereof, or a fragment of SEQ ID NO:6 or a polymorphism thereof.

4. (Original) The method of claim 1, wherein the method comprises analyzing the biological sample for hypomethylation of both a DMR of the H19 gene and a DMR of the IGF2 gene.

5. (Original) The method of claim 2, wherein the DMR of the IGF2 gene comprises SEQ ID NO:1.

6. (Original) The method of claim 3, wherein the DMR of the H19 gene comprises SEQ ID NO:6.

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7. (Currently Amended) The method of claim 3, wherein the H19 DMR comprises a CTCF binding site, <u>wherein the binding site comprises nucleotides</u> ~~7855-8192~~ <u>3010-3172 of SEQ ID NO:6</u>.

8. (Currently Amended) The method of claim 3, wherein the analysis is performed by contacting the biological sample with a primer pair comprising ~~at least one pair of:~~
   ~~SEQ ID NO:7 and SEQ ID NO:8;~~
   ~~SEQ ID NO:9 and SEQ ID NO:10;~~
   ~~SEQ ID NO:11 and SEQ ID NO:12;~~
   ~~SEQ ID NO:13 and SEQ ID NO:14;~~
   ~~SEQ ID NO:15 and SEQ ID NO:16;~~
   ~~SEQ ID NO:17 and SEQ ID NO:18;~~
   ~~SEQ ID NO:19 and SEQ ID NO:20;~~
   ~~SEQ ID NO:21 and SEQ ID NO:22.~~
   SEQ ID NO:23 and SEQ ID NO:24;
   ~~SEQ ID NO:25 and SEQ ID NO:26;~~
   ~~SEQ ID NO:31 and SEQ ID NO:32; and~~
   ~~SEQ ID NO:33 and SEQ ID NO:34.~~

9. (Withdrawn) The method of claim 2, wherein the analysis is performed by contacting the biological sample with a primer pair comprising at least one pair of:
   SEQ ID NO:2 and SEQ ID NO:3;
   SEQ ID NO:4 and SEQ ID NO:5;
   SEQ ID NO:27 and SEQ ID NO:28; and
   SEQ ID NO:29 and SEQ ID NO:30.

10. (Currently Amended) A method for identifying an increased risk of developing cancer in a human subject, comprising analyzing a biological sample from the subject for

hypomethylation of a differentially methylated region (DMR) of an H19 gene or an IGF2 gene, wherein detection of hypomethylation of the DMR in the subject correlates with loss of imprinting (LOI), and wherein LOI is indicative of increased risk of the subject developing cancer.

11. (Original) The method of claim 10, wherein the cancer is colorectal cancer.

12. (Withdrawn) The method of claim 10, wherein the methods comprises bisulfite genomic sequencing performed using the primer pair SEQ ID NO:23 and SEQ ID NO:24, followed by the primer pair SEQ ID NO:25 and SEQ ID NO:26.

13. (Original) The method of claim 10, wherein the subject is not a subject known to have a colorectal neoplasm.

14. (Original) The method of claim 10, wherein the H19 DMR comprises SEQ ID NO:6 or a polymorphism thereof, or a fragment of SEQ ID NO:6 or a polymorphism thereof and the IGF2 DMR corresponds to SEQ ID NO:1 or a polymorphism thereof, or a fragment of SEQ ID NO:1 or a polymorphism thereof.

15. (Original) The method of claim 10, wherein the method comprises analyzing the biological sample for hypomethylation of a differentially methylated region (DMR) of an H19 gene and an IGF2 gene.

16. (Original) The method of claim 10, wherein the biological sample is a blood sample.

17. (Currently Amended) A method for identifying an increased risk of developing cancer in a subject, comprising analyzing a first genomic DNA biological sample from the subject for hypomethylation of a IGF2 gene, wherein hypomethylation of the IGF2 gene correlates with the loss of imprinting of the IGF2 gene, and wherein a loss of imprinting of the

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IGF2 gene is indicative of an increased risk of developing cancer, thereby identifying an increased risk of developing cancer in the subject.

18. (Original) The method of claim 17, wherein the cancer is colorectal cancer.

19. (Canceled)

20. (Currently Amended) The method of claim 17[[9]], wherein hypomethylation is analyzed for at least one of an H19 DMR comprising SEQ ID NO:6 or a polymorphism thereof, or a fragment of SEQ ID NO:6 or a polymorphism thereof, and an IGF2 DMR comprising SEQ ID NO:1 or a polymorphism thereof, or a fragment of SEQ ID NO:1 or a polymorphism thereof.

21. (Withdrawn) A kit for determining a methylation status of a differentially methylated region (DMR) of IGF2 or H19, comprising one or more primer pairs corresponding to one or more of:
    SEQ ID NO:2 and SEQ ID NO:3,
    SEQ ID NO:4 and SEQ ID NO:5,
    SEQ ID NO:23 and SEQ ID NO:24,
    SEQ ID NO: 25 and SEQ ID NO:26,
    SEQ ID NO:27 and SEQ ID NO:28, and
    SEQ ID NO: 29 and SEQ ID NO:30.